SOP 11a Associated Document 1: Costing MHRA-regulated studies

This guidance document is concerned with costings for Medicines and Healthcare products Regulatory Agency (MHRA)-regulated clinical research studies.
It may also be useful for costing other types of clinical research studies.
Please always involve the Good Clinical Practice (GCP) managers in the costing of all MHRA regulated studies.

General Considerations for all MHRA-regulated studies

Cost Type	Considerations	Suggested Costing (All staff time is through the study unless otherwise stated)
Staff Costs		
Chief Investigator (CI)/ Principal Investigator (PI) Time	The CI must have protected time to complete their study responsibilities and maintain oversight of the study. This must be reflected in the grant application with a percentage of their salary costed as protected time to work on the study.	At least 5 hours per week. As per Pre Award guidance on organisational minimum requirements
Statistician time Mandatory	The study statistician must have protected time to complete statistical activities for the study. This must be reflected in the grant application with a percentage of their time costed as protected time to work on the study.	As appropriate within the study design
Trial Coordinator Mandatory	All MHRA-regulated study must be supported by a study manager or coordinator. It is not permitted for a medical professional or an academic staff member to act as the study coordinator. . The study manager/coordinator must be at least Queen Mary Academic grade 5/ Barts Health band 6-7, and higher grades are recommended for multicentre or complex studies.	At least 50% whole time equivalent (WTE). Increase WTE if the study is multicentre and/or the coordinator will also be responsible for monitoring.
Database programmer Mandatory	A database programmer will be required to set up, validate and maintain the study database. They will be involved through the life of the study - updating the database to incorporate protocol amendments and locking the data prior to analyses. Depending on the type of service used, the database programmer may be included in the cost of the database (see *Database* section) or they may be costed separately. In rare cases the trial coordinator may be able to fulfil the role of the database programmer.	Obtain estimate from database programmer if not included as part of Clinical Trials Unit (CTU) involvement
Monitoring Mandatory	All MHRA-regulated studies must undergo on-site monitoring. Every host site must be monitored, as must clinical trial laboratories when they are	At least 50% WTE. Increase WTE if

	completing research activities that are not accredited by UKAS or a similar body. Other vendors may also need to be monitored on a case by case basis. The intensity of monitoring will vary depending on the nature of the study. Discuss the study with the Joint Research Management Office (JRMO) GCP & Governance Manager to agree the planned frequency of monitoring visits. The JRMO will monitor single-site studies taking place at either Barts Health NHS Trust (Barts Health) or Queen Mary University of London (Queen Mary). All multi-centre studies must have their own monitor – which could be the Trial Coordinator or another member of staff. Self-monitoring by site teams is not permitted. Monitoring activities may include remote monitoring, but some on-site monitoring will always be required. The monitor must be at least Queen Mary grade 4 / Barts Health band 6, and higher grades are recommended for multicentre or complex studies.	the trial has many sites. Include travel costs for all monitoring visits.
Study Set-up	Research Teams timelines costed to include study set-up. This could be at least 3 month, ideally 6 months.	
Partners and Support Departments		
Site Costs	All clinical trial activities that host sites will be required to complete must be clearly defined in the grant application. If the study involves NHS sites, then the NHS costing team should be involved at an early stage to ensure accurate costing. NHS costs will follow the National Institute for Health Research (NIHR) costing procedures. Each activity will be attributed as either a Research Cost, Treatment Cost or Service Support Cost according to the *Attributing the costs of health and social care Research & Development (ACORD)* guidelines. The research team must determine which activities are standard of care and which are extra research procedures. Pharmacy set should be considered. Most research costs must be paid for by the research grant and so must be included in the grant application. This must be authorised and signed by the Barts Health Accord specialist.	Dependent on study design.
Database Mandatory	The central database used to store data generated by the clinical trial must comply with the requirements of ICH GCP/ISO14155 GCP and the EMA *Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials*. This means that the database must meet a range of requirements including being located on a secure server, being validated prior to use, being backed up regularly and maintaining a full audit trail. See *JRMO SOP 38b Electronic data management systems for MHRA-regulated studies* for further guidance. For Queen Mary sponsored studies, the database should normally be hosted with the School of Medicine and Dentistry (SMD) Safe haven the cost of this should be included if the Institute is not fully integrated. Established units may choose to reflect this case as a staff cost for a database programmer (see *Database Programmer* section).	Obtain an accurate quote from database provider. If not possible, allow £20,000 for database provision.

	It will not normally be permissible to use programs like Microsoft Excel. The database must still be configured and validated for the study, so costs for this work must still be included.	
Vendors	Identify the vendors that you will need to use to complete the study – for example external laboratories, Investigational Medicinal Products (IMP) suppliers and packagers, randomisation and blinding services. Obtain quotes from each vendor and include them in the grant. Please remember all vendors will need to be vendor assesses for suitability – contact your GCP manager. Check with the JRMO to confirm VAT arrangements and **Check the vendor quotes include VAT or else add 20%.** Please refer to your organisation's procurement guidelines for the number of quotes you must obtain before selecting a vendor.	Obtain accurate quote from each vendor wherever possible. If in doubt add 20% for VAT
Clinical Physics Review Mandatory	The Barts Health Clinical Physics review and approve the use of all medical devices and equipment used within clinical trials, unless they are already owned by Barts Health and being used according to their CE mark or UKCA mark. The costs of review vary depending on the work that must be completed. Please see the Clinical Physics costing document for full details. File location: Q-Pulse/Document*Physics*/Clinical Physics/Procedures & Policies	£495 - £4235 depending on activity.
Pharmacy & radiology technical review fees	If you will use the HRA's Pharmacy or Radiology technical assurance services during your application for HRA approval, you will be charged £500 per review completed. Note that this fee also applies to amendments that require technical review.	£500 per review CRE / MPE is £500 each
Insurance	Queen Mary may need to take out additional insurance premiums if the University's standard clinical trials insurance policy does not cover the trial activities e.g. modification or use of device outside of its terms and conditions of use and manufactures warranty Additional Insurance will be necessary if a trial is opening outside the UK and must be identified at an early stage of costing. There will be no additional insurance expenses for Barts Health sponsored studies because Barts Health cannot take our insurance and can only sponsor trials that can be indemnified by the NHS Indemnity Scheme.	Confirm with JRMO whether any additional premiums are required.
Archiving	Studies sponsored or hosted by Barts Health must use the trust's corporate records management centre. Studies sponsored by Queen Mary may use the trust's corporate records management centre, or may identify a suitable alternative and agree it with the JRMO. See *JRMO SOP 20 Archiving* for further details and costs. If data must be archived electronically, Barts Cancer Centre's Archiving service may be used. Please contact Jonathan Croft @ j.croft@qmul.ac.uk for more information and costs. Please include a basic archiving cost for all external NHS and NON NHS Sites. This will be included in the NHS cost according to the NIHR tariff if required. Consider international sites separately.- Obtain these costs from the sites up front to ensure they are included in the grant application.	See the relevant documents to determine the costs of archiving. Archiving is charged on a per box basis at £620 pb

	Study documentation must be archived in accordance with the sponsor's archiving policy – 25 years for Clinical Trial of an Investigational Medicinal Products (CTIMP) and 30 years Advanced Therapy Investigational Medicinal Products (ATIMP)	
Consumables & Expenses		
Supplies and equipment	If the study requires the use of any supplies or consumables outside of standard clinical care, these should be paid for by the research grant. Sites may be reimbursed, or the supplies may be delivered to sites. If equipment is to be loaned to a site, remember to include delivery and return. Note that the use of some consumables may be included in the cost of those procedures e.g. a blood test costs will include the use of the blood tube or kits Courier costs need to be considered.	Cost of supplies plus cost of transport to sites.
Participant travel	If you will reimburse participants for their travel expenses for study visits, these costs must be included in the grant application. Research Teams should survey your research sites to get an accurate picture of their patient catchment and how much patient travel is likely to cost and be mindful that some patients may travel long distances for specialist care.	Careful estimate of expected patient travel costs.
Staff travel/ accommodation	Consider the costs of staff travel and possible accommodation costs, including travel for site initiation visits, monitoring visits, close-out visits, investigator meetings, trial committee meetings and conferences. Check funder Terms and Conditions – example Wellcome Trust will no longer fund flights.	Full costs of staff travel
Dissemination costs	If you intend to publish your results in a publicly accessible form, you may need to pay a fee to the publisher to do so. If you intend to present your findings at a conference then you will have to pay an entry fee and travel costs. If you are required to make your dataset publicly accessible then there may be costs associated with doing so. There may also be costs associated with disseminating your findings to patients and the public – e.g. generating newsletters or organising a patient event.	Dependent on plans for dissemination

Specific Considerations for CTIMPs

Cost Type	Considerations	Suggested Costing
MHRA Application Fee	See the MHRA's website for current application fees. The full application fee is payable when an IMP Dossier will be submitted with the Clinical Trial Application. The reduced fee is payable when an IMP Dossier is not required – e.g. if a cross-referral letter is submitted instead, or all IMPs are licensed and drawn from local hospital stock.	Check MHRA website. At time of writing: Full fee £3366 Reduced fee £248
MHRA Amendment Fee	The amendment fee is payable for each substantial amendment to the clinical trial that requires approval by the MHRA. See page 65 of the MHRA GCP Guide for guidance on which amendments should be submitted to the MHRA. Allow for two substantial amendments per year that the study will be open or in follow-up.	Check MHRA website. At time of writing, fee is £248 per amendment. Allow for two amendments per year.
MHRA Assessment of annual safety reports	MHRA reserve the right to invoice for the assessment of annual safety reports	Check MHRA website. At time of writing, fee is £248 per year
IMP Costs	IMP costs where identified may be included in the grant application or the IMP may be provided by the manufacturer free of charge. If the manufacturer is providing the IMP, it is vital that the terms of the supply are agreed and documented up front. It can be very expensive to repackage and label IMP for use in a clinical trial so the supplier should either agree to do so or the costs for doing so should be included in the grant application. There may be costs for IMP supply even if the IMP will be drawn from local hospital stocks. In controlled trials, the placebo or control intervention must also be costed. The costs for buying high-quality placebos can be expensive - the placebo must be indistinguishable from the active drug. Storage of IMP needs to be considered and costed appropriately. No GP's surgery's to be used for IMP Storage. These costs must be discussed with Costing, GCP and Pharmacy	Dependent on IMP
IMP Packaging and labelling	Unless IMP is drawn from local hospital stocks, it must be packaged and labelled for use in clinical trials. The packaging and labelling are regulated as manufacturing activities and so must be completed in a facility with a manufacturing licence that complies with Good Manufacturing Practice requirements. The finished product must undergo Qualified Person release prior to transport to sites.	Obtain quote from suitable vendor, It is not advisable to estimate this cost, it this needs to be estimated please allow £100,000.
Sponsor Pharmacy Fees	The Barts Health clinical trials pharmacy provides expert advice and for all CTIMPs sponsored by Barts Health or Queen Mary. Contact the sponsor pharmacist to confirm the fee for this service and include it in the grant application.	Contact sponsor pharmacist for cost.

Questionnaire licencing fee	Consider which questionnaires you intend to use- few are free of charge. Obtain quotes from the owner of the questionnaire and include the full licencing fee in the grant application.	Obtain quote from suitable vendor or allow £1,000 per questionnaire
GCP Training	All staff working on clinical trials must undergo ICH GCP training prior to completing trial-specific activities. Staff working on behalf of the study sponsor must complete the JRMO's GCP training course and complete a JRMO GCP refresher every two years. Staff working on behalf of a host site only may complete GCP training from other trusted providers such as the NIHR. Staff at partner organisations must complete GCP training. It is important to set this expectation up front when contracting with vendors. If a vendor requires reimbursement to complete GCP training then they should provide the costs for this in their quote. In some cases – such as support departments – it may be acceptable for a named individual to complete formal GCP training and to disseminate the relevant information to other team members within the department. This should be agreed with the sponsor up front and the proportionate training must be documented in the study file.	Free from the JRMO or NIHR. Partners to provide cost if necessary

Specific considerations for Clinical Investigations of Medical Devices

Cost Type	Considerations	Suggested Costing
MHRA Application Fee	Check the MHRA website to confirm the current fee. The MHRA application fee depends on the Class of the device.	Check MHRA website. At time of writing: Class I, IIa, or IIb other than implantable or long-term invasive devices - £7472 Class IIb implantable or long-term invasive, Class III, and active implantable devices - £15,627
MHRA Amendment Fee	Check the MHRA website to confirm the current fee. The MHRA application fee depends on the Class of the device. Allow for two amendments per year that the Investigation will be open or in follow-up.	Check MHRA website. At time of writing: Class I, IIa, or IIb other than implantable or long-term invasive devices - £207 Class IIb implantable or long-term invasive,

		Class III, and active implantable devices - £331
Device Manufacturing	Production and supply of the Investigational devices may be included in the grant application or the device manufacturer may provide the devices free of charge. Neither Barts Health nor Queen Mary can act as a medical device manufacturer. Therefore a manufacturing partner must be identified to produce the devices. The manufacturer must be named on the IRAS application and must fulfil a number of regulatory responsibilities – see *SOP 9 Sponsorship of clinical investigation and other MHRA-Regulated medical device studies* for further information. If the device manufacturer will charge the sponsor for their involvement in the study then these costs must be included in the grant application or an alternative means of reimbursement (e.g. shared intellectual property) must be agreed.	Dependent on Investigational Devices and manufacturer.
Device Management and usage of.	If there are any consumables required to operate or maintain the device then they should be included in the grant application - e.g. adhesive tape, sterilisation fluid, single-use needles. Should a device be modified in any way that is outside its terms of usage this will invalidate the Insurance and manufacturer's warranty. Please see Insurance section. Staff training on the use of the device may often be incorporated into site initiation visits. But in some cases, more detailed technical training may be required. Such training may need to be costed separately. The costs associated with transporting or destroying the investigational devices at the end of the Investigation should be included in the research grant if not covered by the device manufacturer.	Dependent on Investigational Device.
Investigational software costs	If the Investigational device incorporates or requires novel software to function, there may be costs associated with setting up and maintaining the software e.g. validating the software after installation and after configuration, hosting the software on a secure server etc. See *JRMO SOP 38a Use of Computerised Equipment in Research Studies* for more information.	Dependent on Investigational Device.
ISO14155 Training	All research team members must complete ISO14155 GCP training prior to working on a Clinical Investigation. This is separate from ICH GCP training and applies the principles of Good Clinical Practice to Clinical Investigations of devices. The NIHR do not currently offer ISO 14155 GCP training. The JRMO does offer ISO 14155 training but researchers should be aware that should they not be able to attend this an external training provider must be commissioned. A 2 yearly refreshers are also needed.	Various training providers are available. Allow £400 per staff member.
ISO14155 Licence Fee	ISO14155 is available online from Queen Mary's digital library and is accessible to Queen Mary staff and those with honorary contracts with Queen Mary. But it is not permitted to download and share the document with staff outside Queen Mary. Therefore if other staff are involved in the study, it may be necessary to buy additional licences for the ISO14155 document.	Check ISO website for pricing options.
Patenting and Intellectual Property Costs	In many cases, protections must be in place to secure the intellectual property relating to the design of the experimental device, and these protections will carry costs. Consider whether any such costs should be included in the grant application for the device.	Contact Queen Mary Innovations to seek advice on expected costs.
Regulatory consultant fees	There are a number of technical documents that must be prepared and submitted to the MHRA as part of the Clinical Investigation application. The investigational device should also have a technical file that will ultimately be submitted to the notified body to	Obtain quote from vendor.

	obtain approval to place the device on the market. If the device manufacturer is not responsible for these activities then it may be necessary to contract a	

Specific Considerations for Clinical Trials and Clinical Investigations involving laboratories

Compliance to standards	Laboratories must comply with the requirements of ICH GCP/ISO14155 GCP and the EMA *Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples*. Therefore there are a number of additional requirements that laboratories must fulfil. NHS laboratories completing UKAS accredited activities will already comply with these requirements, but academic or commercial research laboratories may need to do significant additional work to comply with GCP. For example in ensuring that all computer systems are validated, that all staff have proportionate GCP training and that a Quality Management System (QMS) is in place. The laboratory must understand the GCP & EMA requirements and adjust its quote accordingly if it needs to make significant adjustments to comply with the requirements. *JRMO SOP 43 Laboratories* for more information. Specific costs are broken down below.	Obtain accurate quote from the laboratory ensuring that they understand all of the GCP & EMA requirements.
GCP Training	All laboratory staff working on clinical trial activities must complete GCP training proportionate to their role. See the ICH GCP / ISO14155 GCP training guidance in the CTIMP/Clinical Investigation sections for more information.	See ICH GCP / ISO GCP sections.
Laboratory File Maintenance	Each central laboratory should maintain a study-specific laboratory file, similar to an Investigator Site File. The laboratory file should be set up prior to the start of the study, updated throughout the study and archived at the end of the study. While some documents in the laboratory file will be provided by the coordination team, it is likely that a lab will need to produce new documentation as well. The contents of the laboratory file should follow the JRMO Laboratory File Contents Page (*JRMO SOP 43 Laboratories* associated documents).	Obtain quote from lab.
Monitoring Access	Central laboratories will be monitored by the Clinical Trial Monitor and may also be selected for sponsor audit or competent authority inspection. The extent of the monitoring will be determined by the study Risk Assessment and documented in the study monitoring plan. The laboratory must agree to this and provide a quote up front if they require reimbursement for their time.	Obtain quote from lab.
Computer System Validation	All computer systems storing clinical trial laboratory data should undergo an appropriate level of validation prior to their use. If the laboratory's existing systems have not been validated then they should either undergo validation or new systems should be installed and validated. The computer system validation should be completed in accordance with *JRMO SOP 38b Trial Data Management Systems.*	Obtain quote from lab.
QMS	The laboratory must have a QMS to ensure the quality of all clinical trial activities. The laboratory should have a suite of Standard Operating Procedures (SOP) to cover their activities, which may be supplemented with study-specific procedures.	Obtain quote from lab.

	There should be Quality Assurance (QA) personnel in place to oversee the QMS and ensure compliance through training and internal audits. There should also be Quality Control (QC) procedures in place to confirm the accuracy of test results.	
Facilities and equipment maintenance	All equipment and facilities used for study activities must undergo suitable calibration, user acceptance testing and maintenance. If samples need to be stored at specific temperatures then there must be temperature monitoring systems in place.	Obtain quote from lab.
Sample Transport & courier costs	Biological samples must be transported from host sites to laboratories using a suitable method such as a courier. In some cases, samples must be temperature controlled and monitored throughout transit. Sample transport costs must be included in the grant application, unsuitable methods of transport such as public transport will not be accepted.	Obtain quote from vendor. Try to use a preferred supplier when possible
Method Validation	The laboratory will be required to demonstrate how the methods used in the study have been selected and validated prior to the start of analysis. The fees for doing so should be included in the costing, but additional charges may need to be considered if the proposed method cannot be validated. The fees associated with failed or complex method validations should be agreed and included in the grant application.	Obtain accurate quote from the laboratory and agree arrangements for failed or complex method validation.
Repeat Analysis	The requirements for repeat analyses should be agreed with the laboratory. The laboratory should provide quotes for repeat analysis. The cost may be different depending on the reason for the repeat analysis.	Obtain quote from lab.
Blinding and reporting arrangements	Additional arrangements may need to be put in place to ensure that the blind is maintained – for example reporting the results of laboratory tests in an alternative way. It may also be necessary to expedite the reports of some tests if they have the potential to provide	Obtain quote from lab.

Specific Considerations for International Clinical Trials and Clinical Investigations

Cost Type	Considerations	Suggested Costing
National Coordinating Centres	Each host country must have a National Coordinating Centre (NCC) that acts as a central contact point for the sponsor and host sites within the country. The NCC is responsible for obtaining regulatory approvals within the country, setting up host sites and will often be responsible for monitoring. Host countries may also require a sponsor legal representative. A single sponsor legal representative may represent the sponsor for the entire European Economic Area. The NCC- and Sponsor Legal Representative may be the same organisation but they do not have to be.	Obtain quotes from partner organisations.
Sponsor Legal Representatives	Host countries may also require a sponsor legal representative. A single sponsor legal representative may represent the sponsor for the entire European Economic Area. The NCC and Sponsor Legal Representative may be the same organisation but they do not have to be.	Obtain quotes from partner organisations.
Translations	Participant-facing documents should be translated into the local languages of the host countries. Regulatory and study management documents may also need to be translated. Note that regulators and ethics committees may only provide documents	Obtain quoted from partner

	in the local language and so may need to be translated into English for use by the sponsor. Professional translation services should be used.	organisations or vendors.
Global oversight by sponsor	Monitoring and day-to-day oversight may be delegated to national coordinating centres in each country, but the sponsor must maintain overall oversight of the study across all countries and this will likely carry significant costs. For example, the study coordinator should conduct visits of national coordinating centres to confirm their compliance to the protocol and GCP. There may be additional costs associated with international travel, for example visa fees.	Identify all staff and travel costs and other fees.
Additional regulatory costs	Each host country will need to obtain regulatory approval from its medicines regulatory agency and there will be a fee for doing so.	Review regulatory agency websites or obtain costs from NCC.
Additional ethics approval costs	Each host country will have separate requirements for ethics approval. The ethics committees may charge a fee for ethics approval. It is sponsor procedure that all international research must undergo review by a UK ethics committee. If your study is also opening in the UK then it will be reviewed by a UK research ethics committee as part of that process. But if your trial is only opening in international sites then you will need to identify a suitable UK ethics committee to review the trial and some will charge a fee for doing so.	Review ethics committee websites or obtain costs from NCC.
Regulatory compliance costs	There may be additional costs associated with ensuring compliance to the national regulations in each host country. For example, the requirements for IMP labelling, packaging and safety testing may be different in each host country.	Seek advice from NCCs. Obtain a quote from vendors if required.
Import and export fees	There may be additional fees associated with transporting clinical trial supplies to international sites – for example customs charges. This is particularly significant for IMPs and other regulated materials as there may be specific licences required to import or export the sponsor may need to contract a vendor in possession of those licences.	Work with JRMO to identify additional fees. Obtain quotes from vendors if required.
Site costs	Site costs may vary significantly from those of UK NHS sites.	Seek advice from NCCs or directly from prospective sites.